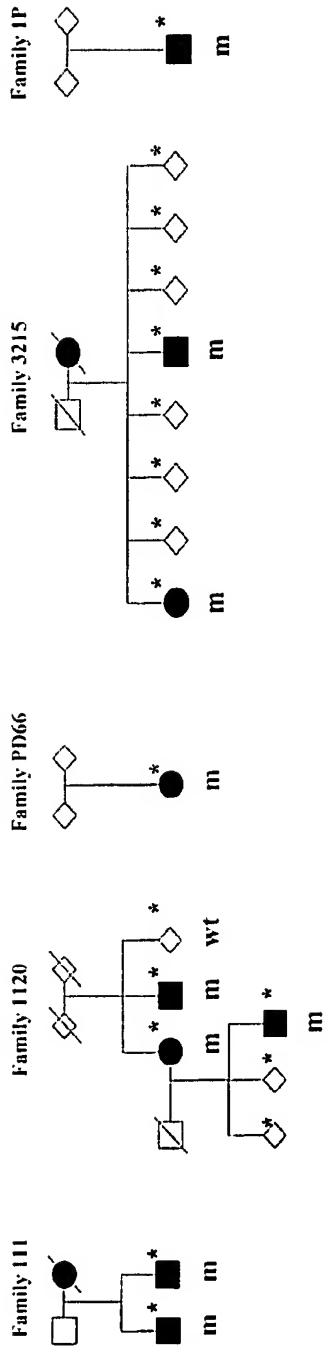
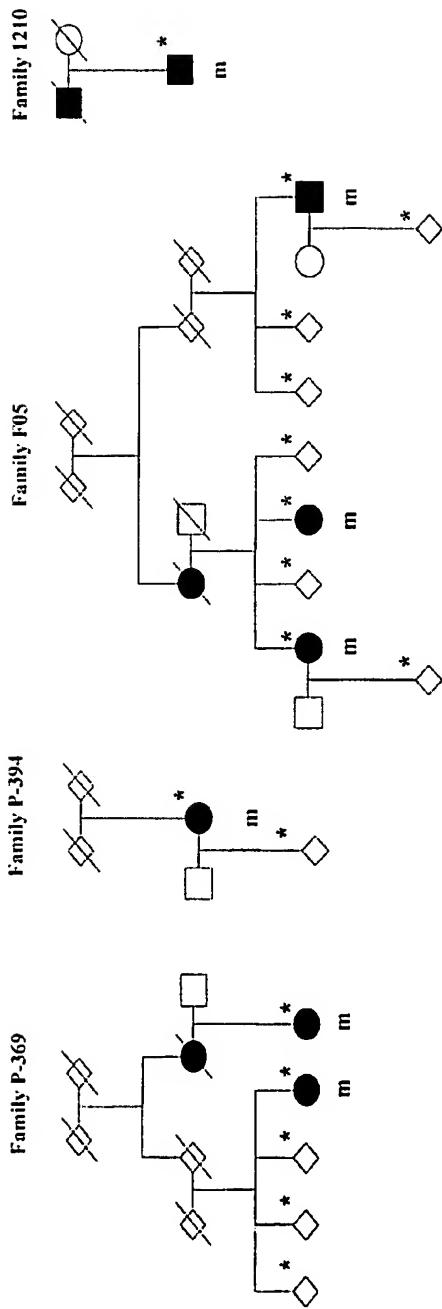
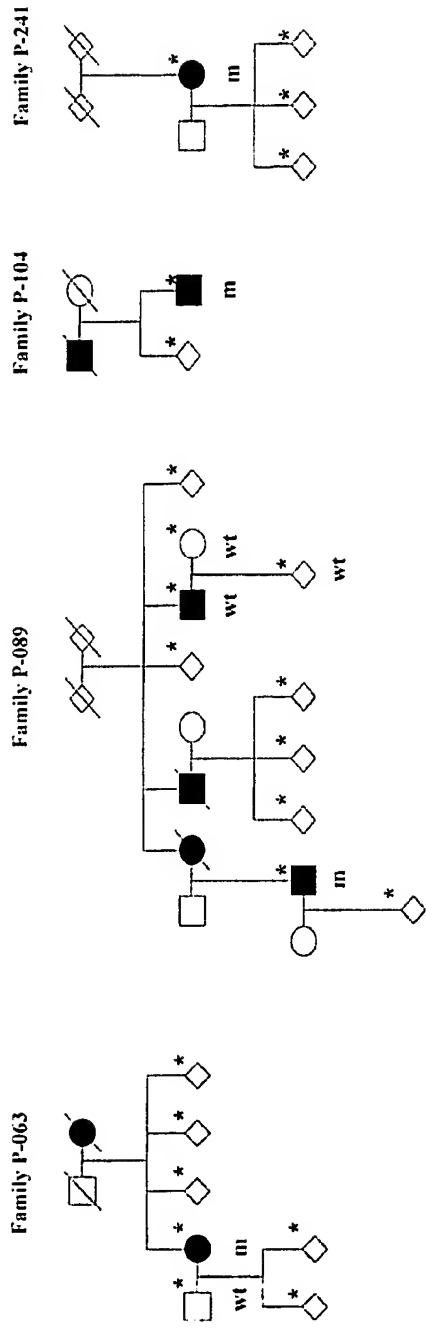


**Figure 1. Schematic drawing of *LRRK2* with predicted protein domains**

(LRR – leucine rich repeat, Roc – Ras in complex proteins, COR – domain C-terminal of Roc, MAPKKK – mitogen-activated protein kinase kinase, WD40 – WD40 repeats). The human *LRRK2* protein sequence in the region of the G2019S mutation is aligned with orthologs from rat (XP\_235581), mouse (AAH34074), frog (AAH76853), and puffer fish (CAG05593). The chromatogram shows the 6055G>A transition (G2019S).



**Figure 2.** Pedigrees of families with *LRRK2* G2019S. □ and ○ denotes sexes, and ∩ denotes that the sex is not given. A diagonal line across the symbol denotes that the person is dead, and thus that he/she has not been tested. Blackened symbols denote affected family members with parkinsonism. An asterisk denotes genotyped individual, with “m” for mutation carriers and “wt” for wild-type *LRRK2*. To protect confidentiality, the genotypes and genders of some unaffected individuals are not shown.



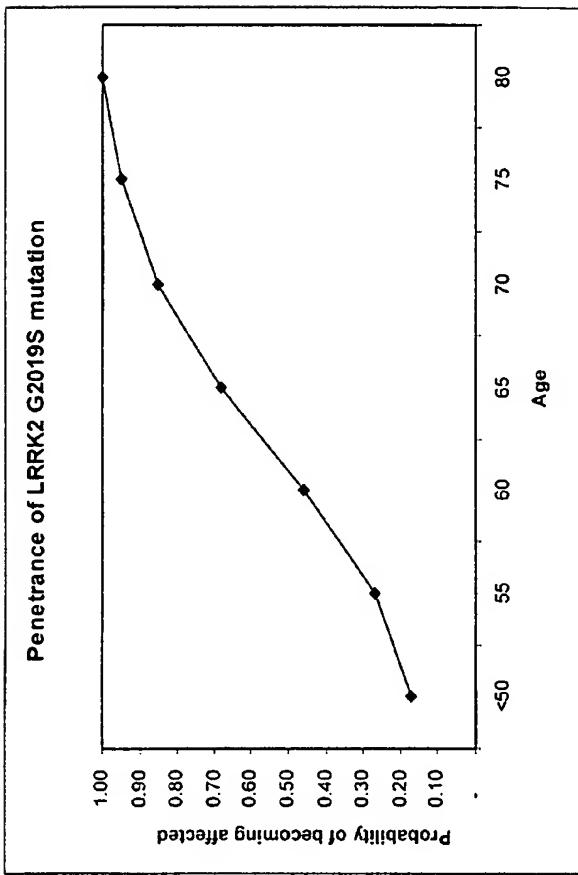
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**Figure 3.** Chromosome 12q12 STR markers on the disease haplotype (PARK8).

Marker	P-063	P-089	P-104	P-241	P-369	P-394	F05	1210	1120	111	3215	PD66	1P
	Family proband												
D12S87	160	160	164	164	-	156	166	156/158	164	160	158	156/166	156/158
D12S1648	120	120	122	122	122	110	110	122/124	110	110	110	120/134	128/130
D12S2080	188	188	188	188	188	188	188	184/192	188	180	184	188/192	184/188
D12S2194	265	265	265	265	265	265	261	253/261	257	257	253	245/249	249/261
-31Kb	290	290	290	290	290	290	290	290/290	290	290	290	290/293	284/293
LRRK2_69Kb	223	223	223	223	223	223	223	219/223	223	223	223	215/215	211/219
LRRK2_34Kb	253	253	253	253	253	253	253	253/253	253	253	253	253/253	253/253
LRRK2_129Kb	151	151	151	151	151	151	151	151/151	151	151	151	151/151	151/151
212Kb	132	132	132	132	132	132	132	132/132	132	132	132	132/138	132/134
243Kb	315	315	315	315	315	315	315	315/315	315	315	315	315/312	315/300
378Kb	189	189	189	189	189	189	189	189/193	193	193	191	183/189	183/187
D12S1048	214	214	214	214	214	214	214	214/223	214	214	223	211/214	211/226
D12S1301	112	116	120	120	116	116	116	108/116	100	120	116	100/116	100/100
D12S1701	95	97	91	91	95	95/97	97	95/101	92	91/95	95	97/101	91/97
Country of origin	United States												Poland
Norway	Ireland												

Genotypes for probands from 13 families with *LRRK2* G2019S are shown; those shared are highlighted in grey.

**Figure 4.** Probability of becoming affected by parkinsonism, in *LRRK2G2019S* carriers, as a function of age.



LRRK2	DYGIAQ-----YCCRMGIKTSSEGTPGFRAPE
LRRK1	DYGISR-----QSFHEGALGVEGTPGYQAPE
MATK	DFGLAK-----AERKGIDSSRILPVVKWTAAPE
PDGFRA	DFGLARDIMHDSNYVSKGSTFLPVVKWMAPE
MAP3K10	DFGLAR-----EWHKTTKMSAACTYAWMAPE
DAPK1	DFGN-----EFKNIFGTPEFVVAPE
BRAF	DFGLATVKSRWSGGSHQFEQLSGSILWMAPE

**Figure 5. Aligned amino acid sequences of the activation loop of different human kinases.**

In most kinases, the activation loop starts and ends with the conserved residues DFG and APE, respectively. In *LRRK2* and *LRRK1* phenylalanine is changed to tyrosine, an amino acid with a similar structure. (LRRK2 – leucine-rich repeat kinase 2, LRRK1 – leucine-rich repeat kinase 1, MATK – megakaryocyte-associated tyrosine kinase, PDGFRA – platelet-derived growth factor receptor alpha, MAP3K10 – mitogen-activated protein kinase kinase kinase 10, DAPK1 – death-associated protein kinase 1, BRAF – v-raf murine sarcoma viral oncogene homolog B1)